REMARKS

I. Amendments

Claims 37, 42, 44, and 49 are pending. Claim 49 has been canceled and new claim 51 has been added. New claim 51 simply represents canceled claim 49 in independent form.

The amendments include no new matter.

II. The rejection of claims 37, 42, 44, and 49 under 35 U.S.C. § 103(a) may be withdrawn.

Claims 37, 42, 44 and 49 stand rejected under 35 U.S.C. § 103(a) as assertedly unpatentable over Kosik et al. (Proc. Natl. Acad. Sci., USA, 1986, Vol. 83, pp. 4044-8) ("Kosik") in view of Harlow and Lane, 1988 (Antibodies, Laboratory Manual, Cold Spring Laboratory, pp. 77, 96-97) ("Harlow and Lane"). Claims 37, 42, 44 and 49 also stand rejected under 35 U.S.C. § 103(a) as assertedly unpatentable over Vooheis, U.S. Patent No. 5,492,812 ("the '812 patent") in view of Harlow and Lane, 1988 (Antibodies, Laboratory Manual, Cold Spring Laboratory, pp. 77, 96-97). In support of the rejections, the Examiner referred to reasons of record in the Office Actions mailed June 10, 2004, and January 31, 2005. Applicants respectfully traverse.

First, with respect to the Examiner's interpretation of the meaning of the phrase "consisting essentially of" as set out in the MPEP, the Applicants submit that the Examiner has misconstrued the legal meaning of this transitional phrase and misapplied MPEP § 2111.03. MPEP § 2111.03 states in relevant part:

> The transitional phrase "consisting essentially of" limits the scope of a claim to the specified materials or steps "and those that do not materially affect the basic and novel characteristic(s)" of the claimed invention (emphasis in original).... For the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, **absent a clear indication in the specification or claims of what the basic and novel characteristics actually are**, "consisting essentially of" will be construed as equivalent to "comprising." (emphasis added).

Thus, the phrase "consisting essentially of" is to be construed to mean "comprising" **only** in the case where the specification **lacks** an indication of what the basic and novel characteristics actually are. To that end, Applicants repeat their assertion that the basic and

novel characteristics are expressly stated in the specification and, as such, the phrase "consisting essentially of" cannot be construed to mean "comprising."

A "basic" and "novel" characteristic of the present invention is that the compositions and methods are useful for the production of antibodies that differentiate between tau protein that is phosphorylated at Serine 262 versus tau protein that is not. In essence, the Applicants are claiming a fragment of full length tau protein which makes up an epitope the Applicants have found significant in diagnosis of Alzheimer's disease. In this condition, serine amino acids at position 262 in tau proteins are hyper-phosphorylated, and an antibody produced using this epitope which can distinguish between the phosphorylated/dephosphorylated state of this residue in tau protein samples from a patient who be extremely helpful in diagnosing the patient's condition.

It is inconsequential whether addition of another amino acid molecule to either end of a fragment would materially affect the basic and novel characteristic(s) of the claimed invention, as suggested by the Examiner. Adding additional amino acids, regardless of the type or source, to the basic structure as claimed does not preclude the fact that the resulting structure, *i.e.,* the fusion protein, would still have the epitope including serine at position 262 which the Applicants have identified to be important in the methods disclosed and claimed. Indeed, it is well known in the art that an isolated epitope when conjugated to additional amino acid sequences increases the immune response against the epitope of interest. Whether the addition amino acids also evoke a response is irrelevant; production of monoclonal antibodies which are immunospecific for a target antigen is well known in the art. *See, e.g.,* Harlow and Lane cited by the Examiner.

With respect to the Examiner's rejection of the claims as assertedly unpatentable over the '812 patent in view of Harlow and Lane, the Applicants again point out that the sections of the '812 patent cited by the Examiner, for example, disclose two large fragments of amino acid residues 1-151 and 154-352. The '812 patent does not disclose or even suggest the specific phosphorylatable fragment/epitope of tau as set forth in the present claims, let alone such a fragment for the purpose of generating an antibody that can distinguish between phosphorylated and dephosphorylated tau. Furthermore, the '812 patent does not provide direction or motivation to those of skill in the art to chose the peptide recited in the present claims from the myriad of possible peptides encoded in SEQ ID NO:2 of

Vooheis. Nowhere in the cited art is the significance of the serine residue at position 262 disclosed as being significant in diagnosis of Alzheimer's disease as set out in the instant specification.

The Examiner will appreciate that the Federal Circuit has held that a fragment of a full length protein is neither the same nor an equivalent of the full length protein. *Genentech v. The Wellcome Foundation* 31 USPQ2d 1161, 1170 (Fed. Cir. 1994) ("[the t-PA fragment] FE1X does not literally meet the limitation - it is not natural t-PA") and *Id.* at 1171 ("... there is undisputed evidence that FE1X behaves significantly differently than human t-PA in the human body.") By analogy, the tau fragment recited in the rejected claims is not literally the tau fragment having amino acid residues 154-352 disclosed in the '812 patent. Nor would the recited fragment function to produce the same antibody response as a fragment having residues 154-352; the larger fragment would generate a much more diverse immune response than a fragment having only the recited epitope. Moreover, as discussed above, the silence in the art as to why any of the disclosures in the cited references should be modified to provide the recited epitope renders moot any assertion of obviousness of the invention as claimed. Simply put, the art does not motivate the worker of ordinary skill to make the presently claimed invention.

In view of the arguments set forth above, the Applicants submit the rejection of claims 37, 42, 44, and 49 under 35 U.S.C. § 103(a), may properly be withdrawn.

III. The rejection of claims 37, 42, 44, and 49 under 35 U.S.C. § 112, second paragraph, may be withdrawn.

At page 4 of the final Office Action, the Examiner claims 37, 42, 44, and 49 under 35 U.S.C. § 112, second paragraph, as assertedly being indefinite. Specifically, the Examiner asserted that claims 37 and 44 are vague because the metes and bounds of an antibody which distinguishes between phosphorylated and dephosphorylated tau cannot be determined from the claims or the specification. Applicants respectfully traverse.

The Examiner asserted that "one skilled in the art readily appreciates that specificity of an antibody is determined by ability to bind to a particular substrate." Applicants agree with the Examiner on this point. Further, one skilled in the art would clearly recognize that the phrase "an antibody which distinguishes between phosphorylated

and dephosphorylated tau" simply means that the claimed antibody binds either phosphorylated tau or dephosphorylated tau, but not both. Whether such a "distinguishing" antibody recognizes the phosphorylated state or the dephosphorylated state is irrelevant; information obtained using either antibody would be the same with a purified tau preparation.

For example, an absence, or low level of binding using an antibody that recognizes tau phosphorylated at residue 262 indicates that residue 262 is dephosphorylated, at least to a large extent, while a high level of binding indicates a high level of phosphorylation. Conversely, an absent or low level of binding with an antibody that recognizes tau dephosphorylated at residue 262 indicate that this residue is highly phosphorylated in the same, while a high level of binding with this antibody would indicate a low level of phosphorylation. Thus, the resulting information is the same. The important aspect of the generated antibody is only its ability to distinguish between the phosphorylation states and this feature is expressly recited in the claims.

In view of the arguments set forth above, the Applicants submit the rejection of claims 37, 42, 44, and 49 under 35 U.S.C. § 112, second paragraph, may properly be withdrawn.

CONCLUSION

In view of the above arguments and amendments, Applicants believe the pending application is in condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue.

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Respectfully submitted,

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